



# Hydroxychloroquine as a Prophylaxis for COVID-19: An Observational Study About Awareness Among the Healthcare Workers

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## ABSTRACT

**Background:** Various modalities are under study for the prevention and treatment of novel coronavirus. One such modality is the use of Hydroxychloroquine/Chloroquine. The objective of the survey was to understand the awareness and impact of HCQ/CQ prophylaxis among the health care workers (HCWs) especially anaesthetists as they are fighting it on the frontline.

**Methods:** A web-based, cross-sectional survey was conducted for HCWs globally. Participation was voluntary and confidentiality was maintained by making participants' information anonymous. The questionnaire consisted of 28 items. Data were tabulated in excel, and descriptive statistics were performed.

**Results:** The survey was taken by 344 HCWs from all over the world. 98% of participants heard about the use of HCQ/CQ prophylaxis against COVID 19 infection. 301 HCWs knew about the side effects of HCQ/CQ. 54.1% of participants agree there is not adequate research done. 122 participants took HCQ/CQ prophylaxis. Out of 29.5% participants who received the medicine from the hospital under hospital protocol, 66.7% were given medication without baseline investigations and 30.5% HCWs were not even briefed about the drug and its side effects by the hospitals. 36.2% of participants developed side effects. 8.7% of HCWs were tested for COVID19 out of 344 participants.

**Conclusion:** The drug taken by HCWs was without adequate evidence, prior investigations, supervision and follow-up. Most of the participants self-prescribed the drug. No separate guidelines were stated for people who had co-morbid conditions. Hospitals neither conducted baseline investigations and nor briefed HCWs about HCQ/CQ. These are some serious concerns we are looking into as who will be answerable in case of adverse events.

**Key Words:** COVID19, Hydroxychloroquine prophylaxis, Healthcare workers, Chloroquine

## INTRODUCTION

Coronavirus is a novel virus which has created the pandemic crisis. Most of the studies that are being done to understand its pathophysiology, course of the disease and its management are either small sample studies or single-arm studies. It has involved everyone in the healthcare system from multipurpose workers to surgeons, fighting on the frontline. Every department in the hospital is serving these patients in their way. Anaesthetists are actively involved not only in operation theatre with these patients under emergency but also are involved in managing these patients in wards and ICU. SARS-CoV-2 seems to have originated from bats and the first report of cases was from Wuhan, Hubei Province in China, suggesting an animal-to-human spread from a live animal market.<sup>1</sup> On March 11, 2020 Coronavirus disease was

declared as a pandemic by the World Health Organization (WHO).<sup>2</sup>

In the current global scenario where every healthcare system of the world is busy in finding the cure through drugs and vaccines, the only definitive management we know is prevention. Prevention by social distancing, hand hygiene and staying at home. Amidst this global chaos, there are a group of people who are out of their houses and serving the needy and the diseased, by risking their lives. This condition in turn has created a panic among these healthcare workers (HCWs) of being getting infected with COVID19. *Fear* is a normal *human* reaction that protects us by signalling danger and preparing us to deal with it. People *tend* to avoid the situations they *fear* or *overcome* it. When a *tendency* to *fear* is present in excess, its consequences are not always helpful.

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The National Task Force for COVID 19 constituted by Indian council of medical research (ICMR) under the ministry of health and family welfare issued the guidelines<sup>3</sup> dated 21<sup>st</sup> March 2020 on the prophylactic use of Hydroxychloroquine/Chloroquine(HCQ/CQ) against SARS-CoV-2 for high-risk population, including asymptomatic healthcare workers involved in the direct care of suspected or confirmed cases of COVID 19. Its use in prophylaxis is derived from available evidence of benefit as treatment and supported by preclinical data.<sup>4</sup> Although some in-vitro evidence supports the antiviral activity of hydroxychloroquine and its precursor chloroquine, there is no peer-reviewed publication that evaluates either drug for exposure prophylaxis of SARS-CoV-2 infection.<sup>4</sup> A letter of correspondence published with The Lancet again quotes that “We are deeply concerned that in this environment of global panic, an endorsement by the highest scientific body of India (and also by the President of the USA) will create an overly optimistic perception of the effectiveness of hydroxychloroquine among the public. Markets in the USA are already reporting a short supply of both hydroxychloroquine and chloroquine. The situation in India is no different, probably indicating widespread self-medication”.<sup>4</sup> A tweet by President Trump on 21<sup>st</sup> March 2020 claiming that “the combination of HCQ and azithromycin has a real chance to be one of the biggest game-changers in the history of medicine” accelerated a worldwide run on the drugs, with pharmacies reporting shortages within 24 hours.<sup>5</sup>

Hydroxychloroquine is a well-established drug that has indications for various diseases like malaria, systemic lupus erythematosus and rheumatoid arthritis. Looking this from a different perspective, the well established are the indications so are the side effects and the precautionary warnings. Ocular manifestations, cardiac side-effects, hypoglycaemia are a few to name.<sup>6</sup>

So to understand the awareness and knowledge of HCQ/CQ among the health care workers in this panic situation, we decided to do a voluntary survey with a set of 30 questions which will help the HCWs to better understand the drug and its impact. Out of the various fields, we chose to study the awareness and impact of HCQ/CQ on health care workers. Seeing the excessive use of HCQ/CQ by the health care workers in the vicinity and the little knowledge they carried about the drug, intrigued us to find out the various aspect of it and hence we started this survey.

## MATERIALS AND METHODS

### Basis, Generation and Propagation of Survey

This survey was conducted at a tertiary-care hospital from 16<sup>th</sup> -30<sup>th</sup> July 2020. A web-based, cross-sectional study was conducted using a survey instrument to obtain responses

from HCWs globally. A 28 item questionnaire survey was generated on an online survey tool, the surveyplanet.com and branching of questions were done to get the targeted results. The question branching controls which questions the participants see based on their responses to previous questions. The link was mailed to the potential responders who included doctors, nurses, technicians and other healthcare staff globally through social networking sites and applications. The total time to complete the survey was estimated to be 3-5 minutes. A total of 344 responders completed the survey. The 28-item questionnaire was divided into 3 sub-headings: Sociodemographics (8 items), Awareness (6 items) and Impact of HCQ/CQ prophylaxis on HCWs (14 items).

### Statistical Analysis

For data collection, the convenient sampling method was used. The distribution of responses was presented as frequency and percentages. Using SPSS 17 data was tabulated in excel, and descriptive statistics were performed.

### Ethical Considerations

The Institutional Ethics Committee (IEC) reviewed and approved the study. Confidentiality of personal information was maintained throughout the study by making participants' information anonymous. Eligible HCWs' participation in this survey was voluntary and was not compensated. Electronic informed consent was shown on the initial page of the survey, such that by taking the survey they automatically consented for the survey. Consent in this study was taken following the Declaration of Helsinki as revised in 2013. This study was conducted as per the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines.<sup>7</sup>

## RESULTS

### Sociodemographics

This survey was taken by 344 HCWs from all over the world with the majority of them being from India. Out of these 344 Healthcare Workers, 40.7% were females, 59 % were male. Maximum HCWs belonged to the age group of 18 to 40 years (64%). Majority of HCWs were from a large tertiary centre (62.2%) and were anesthesiologist/intensivist (32.3%) (Figure 1). Out of 344 HCWs, 222 participants worked in facilities which provided care to suspected /known COVID19 patients and 130 participants were directly involved in their care (Table 1).

### Awareness

HCWs were questioned about their knowledge of Hydroxychloroquine/Chloroquine prophylaxis. 98% participants heard about the use of HCQ/CQ prophylaxis against COVID 19 infection and the most common medium was national/

state guidelines (23.4%). 18.4% participants admitted, they have heard it as word of mouth from colleagues. Overall 49.7% of participants admitted that they were not briefed about the use of HCQ prophylaxis by the hospital (Figure 1).

Total 301 (87.5%) HCWs knew about the side effects of HCQ/CQ. HCWs were asked about the reason for not taking HCQ/CQ prophylaxis and 37.5% participants answered due to the inadequate literature available supporting its use against COVID-19 (Table 2). 15.5 % of participants were scared to use it because of its known side effects. 54.1% of participants think there is not adequate research done on the use of HCQ/CQ prophylaxis against COVID19.

### Impact

Out of 122 participants who took HCQ prophylaxis, 56 participants self-prescribed the drug and remaining were either prescribed by medical practitioners or followed National/State/hospital protocols (Table 3). Among 29.5% participants who received the medicine from the hospital under hospital protocol, 66.7% were given medication without baseline investigations like ECG, G6PD levels and 30.5% HCWs were not even briefed about the drug and its side effects by the hospitals. 49.3% of 122 participants, who took HCQ/CQ prophylaxis, had common co-morbid diseases like hypertension and diabetes mellitus and others. Among 34 (36.2%) participants who developed side effects while on HCQ/CQ only 61.8% of them were sure that it was because of HCQ/CQ, remaining were unaware. Most common side effect observed was headache followed by nausea and vomiting, abdominal pain, anorexia, impaired vision, hypoglycaemia diarrhoea. 4 participants developed chest pain and discomfort. Only 14.7 % of participants who developed side effects consulted a doctor.

65.6% HCWs took 400 mg HCQ twice daily on day 1 followed by 400mg once a week for 7 weeks. Among the total 122 participants who took HCQ/CQ prophylaxis, 83(63.4%) of them did not do any investigation like ECG or G6PD levels before starting HCQ/CQ even though 78 participants were aware of the side effects. Statistically quoting, 60 participants have given HCQ/CQ as prophylaxis to their relatives who are not directly exposed to COVID19 patients. Only 8.7% HCWs were tested for COVID19 out of 344 participants, 2 were confirmed positive and 4 participants were waiting for results.

### DISCUSSION

The world is seeing a pandemic at such a massive scale after the 1918 Spanish Flu. While the scientist and researchers all over the world are engrossed in inventing a vaccine or a treatment for COVID19, it is our moral responsibility to keep things to stop its expansion. In doing so, we may feel perturbed and many things may go wrong although they are

not intended to. This so-called collateral damage needs to be surveyed and controlled. WHO designed Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI) in 2018 after the Ebola virus outbreak.<sup>8</sup>

In our study majority of participants worked in large tertiary hospitals. Almost all of them had heard about HCQ/CQ use as prophylaxis against covid19 infection but their source of information was vague and unreliable. Even though the participants belonged to the specialized group, their knowledge of this trial drug was insufficient. Most of them were aware that the research data on HCQ/CQ use as prophylaxis is very limited but they still took the prophylaxis. One of the reasons could be the bold statements made in news media by the concern authorities and the national and state guidelines recommending the same. The fear of acquiring the infection by this high-risk group led to the widespread use of HCQ/CQ, even by their family members overlooking the harm the drug may cause.

We observed that 36.2% of participants who took the prophylaxis developed the side effects. Only a few of them got tested for taking the medication, which could have lead to deleterious effects. Most of the participants self-prescribed to be safe during the pandemic crisis. After studying these results, we were paralysed with fear that a drug with serious side effects<sup>9</sup> is being taken by HCWs without adequate evidence, prior investigations, supervision and follow-up. In some countries, before conducting a clinical trial on humans, HCQ/CQ was already recommended by the national guidelines.<sup>3</sup> No separate guidelines were stated for people who had co-morbid conditions. Even some hospitals who followed the use of HCQ/CQ prophylaxis protocol to combat COVID 19 did not conduct baseline investigations before giving the medication. Majority of HCWs were not briefed by hospital authorities about HCQ/CQ which is of utmost priority especially during this time of pandemic when there are only drug trials in the name of treatment.

Almost all HCWs who took HCQ/CQ prophylaxis were aware of the side effects but still, very few of them did baseline investigation like ECG, to rule out prolonged QT, which is the common adverse effect of the drug. The social trepidation around COVID19 is so dreadful that the HCWs who are expected to be sane and rational in these difficult times have lost the credence in medicine. This panic has put the HCWs at the risk of self-immolation. There is quite a good number of cases reported where the false assurance of HCQ prophylaxis has led to mortality in the general public as well as HCWs. This falsification has increased the demand of HCQ to such an extent that American College of Physicians has published their concerns and opinions to overcome the scarcity of HCQ for those patients who are already on treatment for illnesses other than COVID19.<sup>5</sup> Not to mention that in vitro studies<sup>10-12</sup> supported by a small study of France<sup>13</sup>



have led to this perplexity. Post-exposure prophylaxis (PEP) was completed in 184 (97.4%) patients and 21 (95.5%) care workers without serious adverse events. At the end of 14 days of quarantine, follow-up PCR tests were all negative. Based on their experience, they implemented PEP with HCQ safely under proper monitoring.<sup>14</sup>

Use of HCQ/CQ as prophylaxis of in COVID-19 is supported by pre-clinical results which are impressive, there is the dearth of evidence supporting the efficacy and safety of CQ or HCQ in preventing COVID-19 infection.<sup>15</sup> Prophylaxis with CQ or HCQ against COVID-19 needs to be thoroughly evaluated in observational studies or high quality randomized controlled studies considering potential safety issues and the likelihood of imparting a false sense of security.

The above-mentioned figures show lacunae in the guidelines and recommendations. Some of the sincere questions arise are- “Why was informed consent advisory not followed as per MEURI? Why not all HCWs were investigated before starting of the HCQ prophylaxis? What are the recommendations for the participants who were hypertensive and diabetic or who were already on HCQ treatment for other illnesses? Why there were no strict guidelines for the hospitals to educate about HCQ and monitor its usage? After starting of prophylaxis why the HCWs were not tested for COVID19, to see if it works as prophylaxis? Finally, after the cacophony created by these events, clinical trials are conducted from the United States of America ( NCT04308668), Spain ( NCT04304053), Europe and Asia (NCT04303507) to name a few<sup>15</sup>. But we are still unsure and blind about it, just hoping once again science saves the world.

Based on these evidences we recommend that the HCWs should be aware and keep them update about the drug trials, its effect and side effect profile before taking any medication as prophylaxis. HCWS should educate themselves about the strength of available data regarding trial drugs in treating COVID-19. The concern authorities should take strict measures to avoid misuse of trial drugs and implement guidelines on its use only under supervision. The hospitals should share the responsibility by educating their HCWs about this new crisis and the treatment modalities available to them. The necessary investigation should be made mandatory before starting a trial drug for prophylaxis or treatment. On the other hand, we believe time plays a major role in these unusual times. And that has restricted us to keep the survey open for a longer duration and more respondents. Furthermore, since this was a cross-sectional study, participants were not followed up.

## CONCLUSION

It was premature to recommend HCQ/CQ as a panacea for prophylaxis of COVID-19 in absence of robust in vivo and

clinical trials. Quarantine, social distancing and personal hygiene seem to be the only proven preventative measures in the current scenario. Furthermore, the pandemic hysteria that caused unrestricted off-label use HCQ/CQ by common people without adhering to the guidelines has led to the deprivation of these essential drugs to other legitimate patients due to mismatch in demand and supply. Thus, further, prudence is warranted in this regard.

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**Conflicts of interest/Competing interests** – No conflict of interests.

**Ethics approval**- The Institutional Ethics Committee (IEC) reviewed and approved the study.

**Consent to participate** - Electronic informed consent was shown on the initial page of the survey, such that by taking the survey they automatically consented for the survey. The study was performed following the Declaration of Helsinki as revised in 2013.

**Consent for publication** – Not applicable

**Availability of data and material** – Partially available

**Code availability** – Not applicable.

**Conflicts of Interest**: None

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**Table 1: Sociodemographic data of the Healthcare workers.**

Demographics			
	Sub – Groups	Frequency	Percentage
Age (years)	18 -40	220	64.0
	40-60	105	30.5
	>60	19	5.5
	Total	344	100.0
Gender	Female	140	40.7
	Male	203	59.0
	Undisclosed	1	0.3
	Total	344	100.0
Country of work when filling in the survey?	Afghanistan	4	1.2
	Antigua and Barbuda	1	0.3
	Bahrain	1	0.3
	Bangladesh	1	0.3
	Canada	1	0.3
	Fiji	1	0.3
	France	1	0.3
	Germany	2	0.6
	India	297	86.3
	Italy	8	2.3
	Malaysia	1	0.3
	Malta	1	0.3
	Mexico	1	0.3
	Saudi Arabia	2	0.6
	Singapore	3	0.9
	Spain	4	1.2
	Ukraine	1	0.3
	United Arab Emirates (UAE)	4	1.2
	United Kingdom (UK)	5	1.5
	United States of America (USA)	5	1.5
	Total	344	100.0

Table 1: (Continued)

Demographics	Sub – Groups	Frequency	Percentage
Speciality or usual place of work	Emergency room	13	3.8
	Hospital wards	44	12.7
	Intensive Care Unit	50	14.5
	Operation Theatre	134	39.0
	Outpatient Department	49	14.2
	Research/Clinical Laboratory	9	2.7
	Others	45	13.1
	TOTAL	344	1.0
Designation	Anaesthesiologist/ Intensivist	111	32.3
	Cleaning and maintenance – operational services	1	0.3
	Dentist	2	0.6
	Doctor in training (Intern/Resident)	19	5.5
	General medical practitioners	40	11.6
	HCW not classified here	18	5.2
	Home based personal care worker	1	0.3
	Midwifery professional	2	0.6
	Nursing professional	32	9.3
	Paramedical practitioner	9	2.6
	Physiotherapist	2	0.6
	Respiratory therapist	4	1.2
	Specialist medical practitioners	103	29.9
	Total	344	100.0
Type of hospital	Community, urban hospital	64	18.6
	Large tertiary teaching hospital	214	62.2
	Other	31	9.0
	Polyclinic	16	4.7
	Remote/regional hospital	19	5.5
	Total	344	100.0
Do you work at a facility that has cared/ is caring for patients with suspected or known COVID-19 infection?	No	122	35.5
	Yes	222	64.5
	Total	344	100.0
Have you provided /providing direct care to the patients with suspected or known COVID-19 infection?	No	214	62.2
	Yes	130	37.8
	Total	344	100.0

**Table 2: Awareness of Hydroxychloroquine/Chloroquine prophylaxis among Healthcare workers tabulated under 6 headings**

AWARENESS			
	SUB - GROUPS	FREQUENCY	PERCENTAGE
Have you heard of HCQ / Chloroquine prophylaxis against COVID 19 infection?	No	7	2.0
	Yes	337	98.0
	Total	344	100.0
If yes, how do you know about HCQ/ Chloroquine prophylaxis? (Multiple answers)	Television	71	20.6
	Pharmacy	16	4.7
	Internet	145	42.2
	Hospital protocol	105	30.5
	National/state guidelines	171	49.7
	Colleagues	135	39.2
	International health organisations	89	25.9
Do you know about the side effects of HCQ/ Chloroquine?	No	11	3.2
	Yes	301	87.5
	Unsure	32	9.3
	Total	344	100.0
Do you think there is adequate research on use of HCQ / Chloroquine as prophylaxis against COVID-19 infection?	No	186	54.1
	Unsure	107	31.1
	Yes	51	14.8
	Total	344	100.0
Have you been briefed about use of HCQ/ Chloroquine for prophylaxis by hospital authorities?	No	171	49.7
	Yes	149	43.3
	Unsure	24	7.0
	Total	344	100.0
Reason for not taking HCQ/CQ prophylaxis	Literature supports its ineffectiveness against COVID19	23	10.4
	Inadequate literature available supporting its use against COVID19	130	58.6
	Non Availability of drug	14	6.3
	Due to its known side effects	55	24.7
	Already taking it for some other co morbid condition	0	0
	Total	222	100.0

**Table 3: Awareness of Hydroxychloroquine/Chloroquine prophylaxis among Healthcare workers tabulated under 13 headings.**

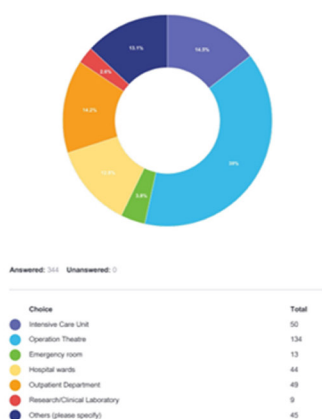
IMPACT		FREQUENCY	PERCENTAGE
	SUB – GROUPS		
Have you taken HCQ/ Chloroquine prophylaxis?	Yes	122	35.5
	No	222	64.5
	Total	344	100.0
Who prescribed you HCQ/Chloroquine prophylaxis?	Hospital Protocol	36	29.5
	Medical practitioner	13	10.7
	National/ State guidelines	17	13.9
	Self	56	45.9
	Total	122	100.0
	200mg HCQ once a day for 2 days, followed by 200mg once weekly for next 14weeks	1	0.8
	200mg HCQ once a day for 2 days, followed by 200mg once weekly for next 7 weeks	5	4.1
Which HCQ / Chloroquine prophylaxis regimen are you following?	400mg HCQ twice a day on day 1, followed by 400mg once weekly for next 3 weeks	28	23
	400mg HCQ twice a day on day 1, followed by 400mg once weekly for next 7 weeks	80	65.6
	Chloroquine 500mg twice daily for 10 days	2	1.6
	Others	6	4.9
	Total	122	100.0
	ECG	38	29
	G6PD levels	10	7.6
Did you do baseline investigations before starting on HCQ/ Chloroquine?(Multiple answers)	None	83	63.4
	Total	122	100
	Hypertension	26	18.3
	Diabetes mellitus	15	10.6
	Ischemic heart disease	1	0.8
	Obesity	8	5.6
	Rheumatic arthritis	2	1.6
Do you have any co morbidities? (Multiple answers)	G6PD deficiency	0	0
	Past history of malaria	9	6.3
	Others	9	6.3
	None	72	50.7
	Total	122	100.0
	Headache	14	10.1
	Chest pain/Discomfort,	4	3.2
Did you develop any of these symptoms while on HCQ/ Chloroquine?(multiple answers)	Anorexia,	3	2.4
	Nausea/vomiting	11	8
	Abdominal pain	9	6.5
	Impaired vision (Ocular complications)	1	0.8
	Others	8	5.8
	None	88	63.8
	Total	122	100.0
Do you think these symptoms were / are due to HCQ/Chloroquine?	No	3	8.8
	Unsure	10	29.4
	Yes	21	61.8
	Total	34	100.0
Did you consult a doctor after developing above mentioned symptoms?	No	29	85.3
	Yes	5	14.7
	Total	34	100.0



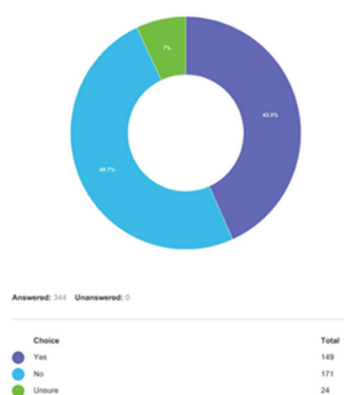
Table 3: (Continued)

		IMPACT	
	SUB – GROUPS	FREQUENCY	PERCENTAGE
Are you presently on HCQ/ Chlo-roquine for treatment of any other illness?	No	326	94.8
	Yes	18	5.2
	Total	344	100.0
Is anyone in your family taking HCQ / Chloroquine?	No	284	82.6
	Yes	60	17.4
	Total	344	100.0
Were you ever tested for COVID 19 Infection?	No	297	86.3
	Not tested, but quarantined	17	4.9
	Yes	30	8.7
	Total	344	100.0
If yes, were you tested positive?	No	24	80
	Waiting for results	4	13.3
	Yes	2	6.7
	Total	30	100.0
	No	28	93.3
Have you taken HCQ / Chloroquine for treatment?	Yes	2	6.6
	Total	30	100.0

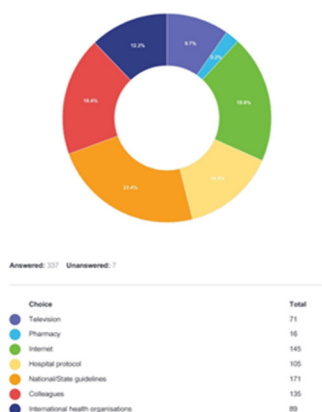
Q7 Usual place of work?\*



Q39 Have you been briefed about use of HCQ/ Chloroquine for prophylaxis by hospital authorities?\*



Q12 How do you know about HCQ/ Chloroquine prophylaxis? (multiple answers)\*



Q14 Who prescribed you HCQ/Chloroquine prophylaxis?\*

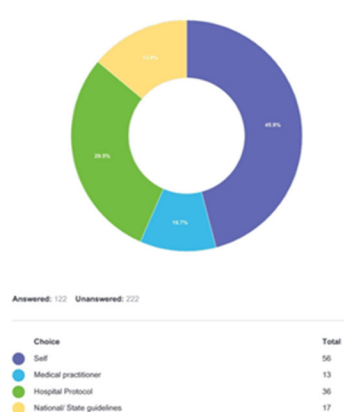


Figure 1: Excerpts of results from Survey.